Claims:

1. An herpes simplex virus wherein the herpes simplex virus genome comprises nucleic acid encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO).

2. An herpes simplex virus according to claim 1 wherein said nucleic acid encodes a mammalian asSCCRO.

3. An herpes simplex virus according to claim 1 wherein said nucleic acid encodes the human asSCCRO.

4. An herpes simplex virus according to claim 1 wherein said nucleic acid encodes a nucleotide sequence complementary to:

(i) the polynucleotide sequence of SEQ ID No.s 1 or 3 or its complement;

(ii) the mRNA transcript of SEQ ID No.s 1 or 3; or

(iii) to a fragment of said polynucleotide sequence or mRNA transcript.

5. An herpes simplex virus according to claim 1 wherein said nucleic acid encodes a nucleotide sequence having at least 60% sequence identity to the nucleotide sequence complementary to:

(i) the polynucleotide sequence of SEQ ID No.s 1 or 3 or its complement;

(ii) the mRNA transcript of SEQ ID No.s 1 or 3; or

(iii) to a fragment of said polynucleotide sequence or mRNA transcript.

6. An herpes simplex virus according to claim 5 wherein said degree of sequence identity is at least 70%.

7. An herpes simplex virus according to any one of claims 4 to 6 wherein a said fragment comprises at least 20 nucleotides and no more than 900 nucleotides.

8. An herpes simplex virus according to claim 1 wherein said nucleic acid hybridises to:

(i) the polynucleotide sequence of SEQ ID No.s 1 or 3 or its complement;

(ii) the mRNA transcript of SEQ ID No.s 1 or 3; or

(iii) to a fragment of said polynucleotide sequence or mRNA transcript

under high stringency conditions.

9. An herpes simplex virus as claimed in any one of claims 1 to 8 wherein said herpes simplex virus genome further comprises a regulatory sequence operably linked to said nucleic acid encoding an antisense to the squamous cell carcinoma related oncogene (as SCCRO), wherein said regulatory sequence has a role in controlling transcription of said asSCCRO.

10. An herpes simplex virus as claimed in any one of claims 1 to 9 wherein said nucleic acid is located in at least one RL1 locus of the herpes simplex virus genome.

11. An herpes simplex virus as claimed in any one of claims 1 to 10 wherein said nucleic acid is located in, or overlaps, at least one of the ICP34.5 protein coding sequences of the herpes simplex virus genome.

12. An herpes simplex virus as claimed in any one of claims 1 to 11 wherein the herpes simplex virus is a mutant of one of HSV-1 strains 17 or F or HSV-2 strain HG52.

13. An herpes simplex virus as claimed in any one of claims 1 to 11 wherein the herpes simplex virus is a mutant of HSV-1 strain 17 mutant 1716.

14. An herpes simplex virus as claimed in any one of claims 1 to 13 which is a gene specific null mutant.

15. An herpes simplex virus as claimed in any one of claims 1 to 14 which is an ICP34.5 null mutant.

16. An herpes simplex virus as claimed in any one of claims 1 to 13 which lacks at least one expressible ICP34.5 gene.

17. An herpes simplex virus as claimed in any one of claims 1 to 12 which lacks only one expressible ICP34.5 gene.

18. An herpes simplex virus as claimed in any one of claims 1 to 17 which is non-neurovirulent.

19. An herpes simplex virus as claimed in any one of claims 1 to 18 wherein said nucleic acid encoding the asSCCRO forms part of a nucleic acid cassette integrated in the genome of said herpes simplex virus, said cassette comprising nucleic acid encoding:

(a) said asSCCRO; and nucleic acid encoding:
(b) a ribosome binding site; and
(c) a marker,

wherein the nucleic acid encoding asSCCRO is arranged upstream (5′) of the ribosome binding site and the ribosome binding site is arranged upstream (5′) of the marker.

20. An herpes simplex virus according to claim 19 wherein a regulatory nucleotide sequence is located upstream (5′) of the nucleic acid encoding asSCCRO, wherein the regulatory nucleotide sequence has a role in regulating transcription of said nucleic acid encoding the asSCCRO.

21. An herpes simplex virus as claimed in claim 19 or 20 wherein the cassette disrupts a protein coding sequence resulting in inactivation of the respective gene product.

22. An herpes simplex virus as claimed in any one of claims 19 to 21 wherein a transcription product of the cassette is a bi- or poly- cistronic transcript comprising a first cistron encoding the asSCCRO and a second cistron encoding the marker nucleic acid wherein the ribosome binding site is located between said first and second cistrons.

23. An herpes simplex virus as claimed in any one of claims 19 to 22 wherein the ribosome binding site comprises an internal ribosome entry site (IRES).

24. An herpes simplex virus as claimed in any one of claims 19 to 22 wherein the marker is a defined nucleotide sequence encoding a polypeptide.

25. An herpes simplex virus as claimed in claim 24 wherein the marker comprises the Green Fluorescent Protein (GFP) protein coding sequence or the enhanced Green Fluorescent Protein (EGFP) protein coding sequence.

26. An herpes simplex virus according to any one of claims 19 to 23 wherein the marker comprises a defined nucleotide sequence detectable by hybridisation under high stringency conditions with a corresponding labelled nucleic acid probe.

27. An herpes simplex virus as claimed in any one of claims 19 to 26 wherein the cassette further comprises nucleic acid encoding a polyadenylation sequence located downstream (3´) of the nucleic acid encoding the marker.

28. An herpes simplex virus as claimed in claim 27 wherein the polyadenylation sequence comprises the Simian Virus 40 (SV4O) polyadenylation sequence.

29. An herpes simplex virus as claimed in any one of claims 1 to 28 for use in a method of medical treatment.

30. An herpes simplex virus as claimed in any one of claims 1 to 28 for use in the treatment of cancer.

31. An herpes simplex virus as claimed in any one of claims 1 to 28 for use in the oncolytic treatment of a tumour.

32. Use of an herpes simplex virus as claimed in any one of claims 1 to 28 in the manufacture of a medicament for the treatment of cancer.

33. A method of lysing or killing tumour cells in vitro or in vivo comprising the step of administering to a patient in need of treatment an herpes simplex virus as claimed in any one of claims 1 to 28.

34. A medicament, pharmaceutical composition or vaccine comprising an herpes simplex virus as claimed in any one of claims 1 to 28.

35. A medicament, pharmaceutical composition or vaccine as claimed in claim 34 further comprising a pharmaceutically acceptable carrier, adjuvant or diluent.

36. An herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO) in at least one of the long repeat regions (R_L).

37. An herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO) and wherein the herpes simplex virus is non-neurovirulent.

38. An herpes simplex virus for use in the treatment of a tumour, wherein the genome of said virus comprises a nucleic acid sequence encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO) in at least one of the long repeat regions (R_L).

39. An herpes simplex virus for use in the treatment of a tumour, wherein the genome of said virus comprises a nucleic acid sequence encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO) and wherein the herpes simplex virus is non-neurovirulent.

40. Use of a herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO) in at least one of the long repeat regions (R_L), in the manufacture of a medicament for the treatment of cancer.

41. Use of a herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO) and wherein the herpes simplex virus is non-neurovirulent, in the manufacture of a medicament for the treatment of cancer.

42. A method for the treatment of a tumour comprising the step of administering to a patient in need of treatment a herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO) in at least one of the long repeat regions (R_L).

43. A method for the treatment of a tumour comprising the step of administering to a patient in need of treatment a herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding an antisense to the squamous cell carcinoma related oncogene (asSCCRO) and wherein the herpes simplex virus is non-neurovirulent.

44. The method of claim 42 or 43 wherein said herpes simplex viruses is capable of killing tumour cells.

45. A method of expressing in vitro or in vivo an antisense to the squamous cell carcinoma related oncogene (asSCCRO), said method comprising the step of infecting at least one cell or tissue of interest with a herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding asSCCRO in at least one of the long repeat regions (R_L), said asSCCRO operably linked to a transcription regulatory sequence.

46. A method of expressing in vitro or in vivo an antisense to the squamous cell carcinoma related oncogene (asSCCRO), said method comprising the step of infecting at least one cell or tissue of interest with a non-neurovirulent herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding asSCCRO, said asSCCRO operably linked to a transcription regulatory sequence.

47. HSV1716asSCCRO (ECACC accession number 04051901).

48. An herpes simplex virus wherein the herpes simplex virus genome comprises nucleic acid encoding a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide.

49. An herpes simplex virus according to claim 48 wherein said siRNA is capable of repressing or silencing expression of a mammalian SCCRO.

50. An herpes simplex virus according to claim 48 wherein said siRNA is capable of repressing or silencing expression of human SCCRO.

51. An herpes simplex virus according to claim 48 wherein said siRNA comprises a nucleic acid of between 10 and 70 nucleotides in length and having the sequence of SEQ ID No.5 or the complement thereof.

52. An herpes simplex virus according to claim 48 wherein said siRNA comprises a nucleic acid of between 10 and 70 nucleotides in length and having at least 70% identity to SEQ ID No.5 or the complement thereof.

53. An herpes simplex virus according to claim 52 wherein said degree of sequence identity is at least 80%.

54. An herpes simplex virus as claimed in any one of claims 48 to 53 wherein said herpes simplex virus genome further comprises a regulatory sequence operably linked

to said siRNA, wherein said regulatory sequence has a role in controlling transcription of said siRNA.

55. An herpes simplex virus as claimed in any one of claims 48 to 54 wherein said nucleic acid is located in at least one RL1 locus of the herpes simplex virus genome.

56. An herpes simplex virus as claimed in any one of claims 48 to 55 wherein the said nucleic acid is located in, or overlaps, at least one of the ICP34.5 protein coding sequences of the herpes simplex virus genome.

57. An herpes simplex virus as claimed in any one of claims 48 to 56 wherein the herpes simplex virus is a mutant of one of HSV-1 strains 17 or F or HSV-2 strain HG52.

58. An herpes simplex virus as claimed in any one of claims 48 to 56 wherein the herpes simplex virus is a mutant of HSV-1 strain 17 mutant 1716.

59. An herpes simplex virus as claimed in any one of claims 48 to 58 which is a gene specific null mutant.

60. An herpes simplex virus as claimed in any one of claims 48 to 59 which is an ICP34.5 null mutant.

61. An herpes simplex virus as claimed in any one of claims 48 to 58 which lacks at least one expressible ICP34.5 gene.

62. An herpes simplex virus as claimed in any one of claims 48 to 57 which lacks only one expressible ICP34.5 gene.

63. An herpes simplex virus as claimed in any one of claims 48 to 62 which is non-neurovirulent.

64. An herpes simplex virus as claimed in any one of claims 48 to 63 wherein said nucleic acid encoding said siRNA forms part of a nucleic acid cassette integrated in the genome of said herpes simplex virus, said cassette comprising nucleic acid encoding :

(a) said siRNA; and nucleic acid encoding:

(b) a first regulatory nucleotide sequence; and

(c) a marker,

wherein the nucleic acid encoding said siRNA is arranged upstream (5′) of the first regulatory nucleotide sequence and the first regulatory nucleotide sequence is arranged upstream (5′) of the marker, wherein said first regulatory sequence has a role in controlling transcription of said marker.

65. An herpes simplex virus according to claim 64 wherein a second regulatory nucleotide sequence is located upstream (5′) of the nucleic acid encoding said siRNA, wherein the second regulatory nucleotide sequence has a role in regulating transcription of said nucleic acid encoding said siRNA.

66. An herpes simplex virus as claimed in claim 64 or 65 wherein the cassette disrupts a protein coding sequence resulting in inactivation of the respective gene product.

67. An herpes simplex virus as claimed in any one of claims 64 to 66 wherein the marker is a defined nucleotide sequence encoding a polypeptide.

68. An herpes simplex virus as claimed in claim 67 wherein the marker comprises the Green Fluorescent Protein (GFP) protein coding sequence or the enhanced Green Fluorescent Protein (EGFP) protein coding sequence.

69. An herpes simplex virus according to any one of claims 64 to 66 wherein the marker comprises a defined nucleotide sequence detectable by hybridisation under high stringency conditions with a corresponding labelled nucleic acid probe.

70. An herpes simplex virus as claimed in any one of claims 64 to 69 wherein the cassette further comprises nucleic acid encoding a polyadenylation sequence located downstream (3′) of the nucleic acid encoding the marker.

71. An herpes simplex virus as claimed in claim 70 wherein the polyadenylation sequence comprises the Simian Virus 40 (SV40) polyadenylation sequence.

72. An herpes simplex virus as claimed in any one of claims 48 to 71 for use in a method of medical treatment.

73. An herpes simplex virus as claimed in any one of claims 48 to 71 for use in the treatment of cancer.

74. An herpes simplex virus as claimed in any one of claims 48 to 71 for use in the oncolytic treatment of a tumour.

75. Use of an herpes simplex virus as claimed in any one of claims 48 to 71 in the manufacture of a medicament for the treatment of cancer.

76. A method of lysing or killing tumour cells in vitro or in vivo comprising the step of administering to a patient in need of treatment an herpes simplex virus as claimed in any one of claims 48 to 71.

77. A medicament, pharmaceutical composition or vaccine comprising an herpes simplex virus as claimed in any one of claims 48 to 71.

78. A medicament, pharmaceutical composition or vaccine as claimed in claim 77 further comprising a pharmaceutically acceptable carrier, adjuvant or diluent.

79. An herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide in at least one of the long repeat regions (R_L).

80. An herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide and wherein the herpes simplex virus is non-neurovirulent.

81. An herpes simplex virus for use in the treatment of a tumour, wherein the genome of said virus comprises a nucleic acid sequence encoding a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide in at least one of the long repeat regions (R_L).

82. An herpes simplex virus for use in the treatment of a tumour, wherein the genome of said virus comprises a nucleic acid sequence encoding a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide and wherein the herpes simplex virus is non-neurovirulent.

83. Use of a herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide in at least one of the long repeat

regions (R_L), in the manufacture of a medicament for the treatment of cancer.

84. Use of a herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide and wherein the herpes simplex virus is non-neurovirulent, in the manufacture of a medicament for the treatment of cancer.

85. A method for the treatment of a tumour comprising the step of administering to a patient in need of treatment a herpes simplex virus, wherein the genome of said virus comprises, in at least one of the long repeat regions (R_L), a nucleic acid sequence encoding a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide.

86. A method for the treatment of a tumour comprising the step of administering to a patient in need of treatment a herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide and wherein the herpes simplex virus is non-neurovirulent.

87. The method of claim 85 or 86 wherein said herpes simplex virus is capable of killing tumour cells.

88. A method of expressing in vitro or in vivo a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide, said method comprising the step of infecting at least one cell or tissue of interest with a herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding said siRNA in at least one of the long repeat regions (R_L), wherein said nucleic acid sequence encoding said siRNA is operably linked to a transcription regulatory sequence.

89. A method of expressing in vitro or in vivo a short interfering ribonucleic acid (siRNA) molecule that is capable of repressing or silencing expression of squamous cell carcinoma related oncogene (SCCRO) nucleic acid or polypeptide, said method comprising the step of infecting at least one cell or tissue of interest with a non-neurovirulent herpes simplex virus, wherein the genome of said virus comprises a nucleic acid sequence encoding said siRNA, wherein said nucleic acid sequence encoding said siRNA is operably linked to a transcription regulatory sequence.